

IN THE SPECIFICATION

Kindly amend the specification as follows.

Page 5, replace the sixth paragraph starting at line 22 with the following:

Figure 3 (a-e) – RNA folds showing predicted secondary structure of SIV_{mac} leader RNA. a) wild type SEQ ID NO:11 b) with $\Delta 1$ mutation SEQ ID NO:12 c) with $\Delta 2$ mutation SEQ ID NO:13 d) with $\Delta 3$ mutation SEQ ID NO:14 e) with $\Delta 4$ mutation SEQ ID NO:15. Positions of deletions are shown in a) by arrows and bold type. Shaded areas indicate sequences corresponding to the primer binding site, dimerisation initiation signal and *gag* initiation codon. Thick lines in b), c), d) and e) indicate position of the deleted sequence.

Page 24, replace the first paragraph starting at line 1 with the following:

For $\Delta 1$, positions 862-898 (numbering from the start of the 5' U3 sequence, or 171-207 when the first base of the R region is numbered 1) were deleted using the mutagenic oligonucleotide 5' AGTGAGAAGAACTCCACCACGACGGACTGC 3' (SEQ ID NO:3).

Page 24, replace the second paragraph starting at line 4 with the following:

For $\Delta 2$, positions 915-947 (or 224-256 on alternative numbering) were deleted using the mutagenic oligonucleotide 5' CCAACCACGACGGAGGCGTGAGGAGCG 3' (SEQ ID NO:4).

Page 24, replace the third paragraph starting at line 7 with the following:

For $\Delta 3$, positions 995-1045 (or 304-354 on alternative numbering) were deleted using the mutagenic oligonucleotide 5' CGGTTGCAGGTAAGTGCAAGTGGGAGATGGGC 3' (SEQ ID NO:5).

Page 24, replace the fourth paragraph starting at line 10 with the following:

For $\Delta 4$, positions 1011-1042 (or 320-351) were deleted using the mutagenic oligonucleotide 5' GCAACACAAAAAAGAGTGGGAGATGGGC 3' (SEQ ID NO:6).

Page 24, replace the sixth paragraph starting at line 15 with the following:

Plasmids used as templates for the production of riboprobes were created as follows: SIVKS Ψ GS used to detect genomic versus spliced RNA was created by amplification of SIV sequences between 818 and 1068 using the primers 5' ATGGGAATTCGTTTCGTTTCTCGCGCCCATCTCCCACTCT 3' (SEQ ID NO:7) and 5'TAATGGATCCAGATTGGCGCCTGAACAGGG 3' (SEQ ID NO:8). The PCR product was then cloned into the *Bam* H1 and *Eco* R1 sites of Bluescript SK + (Stratagene). SIVKSLTR used to discriminate DNA from RNA was created by amplification of SIV sequences between 300 and 750 using the primers 5' CTTTGAATTCACCGAGTACCGAGTTG 3' (SEQ ID NO:9) and 5' TTTGGGATCCTACCCAGAAGAGTTTGG 3' (SEQ ID NO:10) (Figure 2). The PCR product was then cloned into the *Bam* H1 and *Eco* R1 sites of Bluescript SK + (Stratagene).

Page 27, replace the third paragraph starting at line 19 with the following:

We speculated as to whether the $\Delta 4$ mutation might have a more profound effect on the secondary structure of the leader RNA and investigated this using the RNA folding programme [www\(dot\)ibc\(dot\)wustl\(dot\)edu\(backslash\)~zucker\(backslash\)rna\(backslash\)\(~~www.ibc.wustl.edu/~zucker/rna/~~\)](http://www.ibc.wustl.edu/~zucker/rna/). The results are shown in Figure 3 (a-e). Figure 3 shows the RNA structure of the intact region in part a, on which are marked the boundaries of 4 deletion mutants that have been created: at the most extreme 5' end, there is a deletion between the two arrows marked $\Delta P1$; in b, the resulting structure with a bar marks the site of the deleted sequence. The same is true for c for $\Delta P2$ which clearly deletes a structure labelled DIS with some shaded bases (GGUACC) at the tip. Of interest was the fact that the $\Delta 2$ mutation which caused the profound packaging defect deletes an RNA stem loop with a palindromic terminus which would be consistent with part of the leader involved in dimerisation and encapsidation. This remains intact in

the $\Delta 1$, $\Delta 3$ and $\Delta 4$ deletions. These deletions did not cause a packaging deletion indicating that the packaging signal has been precisely identified. The $\Delta 4$ deletion, however, significantly disrupts the structured region between the putative packaging signal/dimer initiation signal loop and the stem loop containing the viral *gag* initiation codon. Although the $\Delta 3$ mutation also disrupts this region, the change in predicted secondary structure is not as severe as that brought about by $\Delta 4$ in which a stem loop present in the wild type and other mutants upstream of the *Gag* initiation codon is replaced by a region of unstructured RNA. We suggest that the dramatic effect of $\Delta 4$ may be caused by the severe disruption of secondary structure, possibly affecting *cis* acting functions other than packaging which are dependent on this region.

LEVER et al. – Appln. No. 10/009,171

IN THE SEQUENCE LISTING

Kindly enter the attached Sequence Listing in lieu of the substitute submitted on May 21, 2002.